REMARKS

As an initial matter, applicants gratefully acknowledge that, while maintaining other parts of the restriction requirement, the Examiner indicated that SEQ ID NO:7 and SEQ ID NO:9 will be examined together.

In the Office Action, the Examiner raised formality objections to the specification and claims 10-14 and 41-50, rejected claims 10-14 and 41-50 for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention, and rejected claims 10-14 and 41-50 as being anticipated by Nishiki et al. 1996 (FEBS Letters 378:253-257) or Nishiki et al. 1994 (J. Biol. Chem. 269:10498-10503). Claims 10, 14, 42, 43, 45, and 47 have been amended. New process claims 51-67 have been added for rejoinder purpose (they depend on the elected product claims). Each objection and rejection raised by the Examiner is addressed separately below. In view of the amendments noted above and the remarks below, applicants respectfully request reconsideration of the merits of this patent application.

No extension of time is believed to be necessary and no fee is believed to be due in connection with this response. However, if any extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. No other fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to the same Deposit Account No. 17-0055.

Objection to the specification

The Examiner objected to the specification stating that the last sentence on page 19 of the application should end in a period. Applicants have added a period to the end of the last sentence on page 19 by amendment and the objection is believed to have been overcome.

Objection to the claims

The Examiner objected to claims 10-14 and 41-50 stating that "BoNT/B" should be changed to "botulinum toxin serotype B" in the first occurrence in the claims. Applicants have amended claim 10 to recite "botulinum toxin serotype B" and the objection is believed to have been overcome.

Rejections under 35 U.S.C. §112-second paragraph

The Examiner rejected claims 10-14 and 41-50 for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. First, the Examiner alleged that it is unclear as to what the term "an amino acid" recited in claim 10 refers. In particular, the Examiner inquired whether applicants meant a subset of the amino acid sequence that is homologous or at least 70% identical to the murine synaptotagmin II BoNT/B binding domain. Applicants respectfully traverse the rejection.

The term "an amino acid sequence" recited in claim 10 is defined by the clause immediately following it, *i.e.*, "that is homologous or at least 70% identical to ...." It is therefore clear that said amino acid sequence itself is homologous or at least 70% identical to a murine synaptotagmin II botulinum toxin serotype B (BoNT/B)-binding domain at amino acid position 40 to 60. If claim 10 recites an amino acid sequence of a polypeptide that is homologous or at least 70% identical to ...," the Examiner's rejection may arguably make sense. However, this is not the case here. The term "an amino acid sequence" is clearly defined by the clause immediately following it. Such claim language has been well established to be acceptable by the United States Patent and Trademark Office. In this regard, applicants refer to the following recently issued U.S. patents (as recent as January 17, 2006) as examples: U.S. patents 6987015 (*see, e.g.*, claim 2), 6949366 (*see, e.g.*, claim 4), 6946274 (*see, e.g.*, claim 1), and 6946271 (*see, e.g.*, claim 2). Withdraw of the rejection is respectfully requested.

Next, the Examiner alleged that it is unclear as to what applicants intend by the term "luminal portion of a synaptotagmin" recited in claim 43. In response, applicants have amended claim 43 to clarify that applicants meant "luminal domain of a synaptotagmin," which is an art-recognized term for the portion of the synaptotagmin that is exposed outside of the cells (*see, e.g.*, paragraph [00066] of the application, lines 1-2). A skilled artisan is familiar with the luminal domains of synaptotagmin proteins. For example, it is provided in the application the luminal domain of a murine synaptotagmin II spans from amino acid 1 to amino acid 60 (*see, e.g.*, paragraph [0007], line 1). The luminal domains of other synaptotagmin proteins, if not already identified, can be readily determined by a skilled artisan through a routine sequence

alignment. In this regard, applicants note that synaptotagmin proteins are highly conserved. It is respectfully submitted that the rejection has been overcome by the amendment.

Next, the Examiner alleged that it is unclear as to what applicants are referring by "wherein the ligand is an antibody or a botulinum toxin fragment" recited in claim 45 given that claim 45 depends on claim 10 which does not include a botulinum toxin component. Applicants respectfully traverse the objection.

It is inaccurate to state that claim 10 does not include a botulinum toxin component. What claim 10 does not include, for example, is a complex of a full length synaptotagmin and a botulinum toxin. A complex of a BoNT/B fragment and a polypeptide consisting of the BoNT/B binding domain of a murine synaptotagmin II, for example, is within the scope of the claim 10. Therefore, it is respectfully submitted that claim 45 is clear.

Lastly, the Examiner alleged that it is unclear as to whether applicants is claiming an organism such as a rat, mouse or human in claim 47 by reciting "wherein the polypeptide is located *in vivo*." In response, applicants have amended claim 47 to clarify that the claim does not cover an organism such as a rat, mouse or human but rather covers a complex that is formed *in vivo* in a mammal. The rejection is believed to have been overcome by the amendment.

Rejections under 35 U.S.C. §102 (b)

The Examiner rejected claims 10-14 and 41-50 as being anticipated by Nishiki et al. 1996 (FEBS Letters 378:253-257) or Nishiki et al. 1994 (J. Biol. Chem. 269:10498-10503). In making the rejection, the Examiner alleged that each of the Nishiki references teaches a complex comprising synaptotagmin II and gangliosides and that the synaptotagmins used in the complex were recombinant synaptotagmins. The Examiner also alleged that the claim limitation "wherein the polypeptide has a sequence identical or homologous to a luminal portion of a synaptotagmin" would be inherent in the teachings of the prior art. Further, the Examiner alleged that the claim limitation "wherein the polypeptide comprises an amino acid sequence that is homologous or at least 70% identical to a murine synaptotagmin II BoNT/B-binding domain at amino acid position 40 to 60 and wherein the ligand binds to the polypeptide at the amino acid sequence that is homologous or at least 70% identical to the murine synaptotagmin II BoNT/B-binding domain at

amino acid position 40 to 60" would be taught by the prior art since the prior art teaches murine synaptotagmin II.

Applicants respectfully traverse the rejection in that the recombinant rat synaptotagmin I and II used in the Nishiki references are the full length rat synaptotagmin proteins and a complex of a full length synaptotagmin and BoNT/B is specifically excluded from the pending claims (see claim 10).

It is well established in the art that when a protein is referred to by its name, as the Nishiki references did by synaptotagmin I and II, the full length protein is intended. Therefore, the recombinant synaptotagmin I and II in the Nishiki references refer to the full length synaptotagmin I and II. The term "recombinant" is used to indicate that the full length proteins were made by recombinant DNA technology rather than by purification from animal tissues.

The description on the recombinant DNA technology in Nishiki et al. 1994 further confirms that the synaptotagmin proteins made are the full length proteins. In this regard, Nishiki et al. 1996 refers to Nishiki et al. 1994 (as reference [7]) for the preparation of recombinant synaptotagmin I and II. In Nishiki et al. 1994 (page 10500, left column under "Expression of Rat Synaptotagmin in *Escherichia coli*"), new restriction sites (*Nde*I and *Bam*HI) were added to the 5' and 3' ends of the coding region of rat synaptotagmin I cDNA and the coding region was cloned into the pET-3a vector via said restriction sites. The integrity of the coding region was then confirmed and vector was introduced into *E. coli* to produce the synaptotagmin protein. A skilled artisan can certainly appreciate from such description that it is the full length synaptotagmin proteins that were being made.

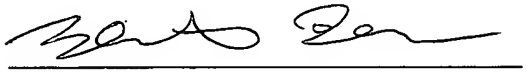
It is clear from the above discussion that the synaptotagmin-BoNT/B complexes disclosed by the Nishiki references are complexes of a full length synaptotagmin and BoNT/B, which is specifically excluded from the pending claims (see claim 10). Therefore, the pending claims are not anticipated by the Nishiki references.

Conclusion

Having addressed each objection and rejection raised by the Examiner, the claims as amended are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issues remain outstanding, the Examiner is invited to contact the

undersigned at the telephone number appearing below if such would advance the prosecution of this application.

Respectfully submitted,



Zhibin Ren
Reg. No. 47,897
Quarles & Brady LLP
411 East Wisconsin Avenue
Milwaukee, WI 53202-4497
Phone (414) 277-5633
Fax (414) 271-3552

QBMKE\5844520.2